

REMARKS/ARGUMENTS

Claims 1-80 were pending in the present application before the amendment as set forth above. By this Amendment, claims 1, 30, 32, 47, 56, 57, 62, 64, 66, 73, 74, 76, 77 and 80 are amended, and claims 46, 65 and 79 are canceled.

The October 8, 2003 Office Action rejected claims 1, 2, 11, 15-17, 20-22 and 77-80 under 35 U.S.C. §102(b) as being anticipated by U.S. Pat. No. 5,118,937 to Hillenkamp et al (hereinafter "Hillenkamp"), claims 1-5, 11, 12, 15-22, 46-48, 56, 64-67, 73 and 76-80 under 35 U.S.C. §102(e) as being anticipated by U.S. Pat. No. 6,104,028 to Hunter et al (hereinafter "Hunter"), and claims 1, 2, 11, 12, 15-17, 20-22 and 77-80 under 35 U.S.C. §102(b) as being anticipated by Krutchinsky et al, Journal of Rometry, 1995, Vol. 30, pp. 375-379 (hereinafter "Krutchinsky").

Furthermore, claims 3-5, 18, 19, 46-48, 51-56, 64-67, 70-73 and 76 were rejected under 35 U.S.C. §103(a) as being unpatentable over Krutchinsky as applied to claims 1, 2, 11, 12, 15-17, 20-22 and 77-80 above, and further in view of Hunter as explained above. Moreover, claims 6-10, 23-29 and 33-45 were rejected under 35 U.S.C. §103(a) as being unpatentable over Krutchinsky as applied to claims 1, 2, 11, 12, 15-17, 20-22 and 77-80 above, and further in view of Strahler et al, International Journal of Mass Spectrometry and Ion Processes, 1997, Vol. 169/170, pp. 111-126, (hereinafter "Strahler"). Additionally, claims 49-55 and 68-72 were rejected under 35 U.S.C. §103(a) as being unpatentable over Hunter as applied to claims 1-5, 11, 12, 15-22, 46-48, 56, 64-67, 73 and 76-80 above, and further in view of Cramer et al, International Journal of Mass Spectrometry and Ion Processes, 1997, Vol. 169/170, pp. 51-67, (hereinafter "Cramer").

However, the Examiner indicated that "claims 30-32, 57-63, 74 and 75 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims."

Applicants very appreciate the Examiner's careful review of the application, and indication of allowability of claims 30-32, 57-63, 74 and 75.

In response, as set forth above, claims 1, 30, 32, 47, 56, 57, 62, 64, 66, 73, 74, 76, 77 and 80 have been amended. Specifically, the word "turned" in claim 1, line 6 has been replaced by "tuned", to correct a typo. Claims 30 and 32 have been respectively rewritten in independent form to include all of the limitations of the base claim, claim 23, and the intervening claim, claim 29. Claims 57 and 62 have been respectively rewritten in independent form to include all of the limitations of the base claim, now canceled claim 46. Claim 74 has been rewritten in independent form to include all of the limitations of the base claim, now canceled claim 65. Furthermore, claims 47, 56 and 64 have been amended to be dependent from amended claim 62, and claims 66, 73 and 76 have been amended to be dependent from amended claim 74. Moreover, claim 77 has been amended to include all of the limitations of now canceled claims 79, and claim 80 has been amended to be dependent from amended claim 77.

Additionally, without acquiescing in the propriety of the Examiner's rejections and to facilitate the prosecution of the current application, claims 46, 65 and 79 have been canceled, which makes the Examiner's rejections under 35 U.S.C. §102(e) and §103(a) to claims 46 and 65, and under 35 U.S.C. §102(b) and §102(e) to claims 79 moot, respectively. Applicants reserve every right in cancelled claims 46, 65 and 79 to file continuation applications.

The following remarks herein are considered to be further responsive thereto.

Support for the amendments set forth above can be found in the disclosure as originally filed. Thus, no new matter is added. However, the claims are not limited to the disclosed embodiments.

Any amendments to the claims not specifically referred to herein as being included for the purpose of distinguishing the claims from cited references are included for the purpose of clarification, consistence and/or grammatical/spelling correction only.

It is now believed that the application is in condition for allowance and such allowance is respectfully requested.

A. Allowable Subject Matter

In the October 8, 2003 Office Action, the Examiner indicated that “claims 30-32, 57-63, 74 and 75 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.”

As set forth above, claims 30, 32, 57, 62 and 74 have been amended according to the Examiner’s suggestions. More specifically, claim 30 has been rewritten in independent form to include all of the limitations of the base claim, claim 23, and the intervening claim, claim 29, claim 32 has been rewritten in independent form to include all of the limitations of the base claim, claim 23, and the intervening claim, claim 29, claim 57 has been rewritten in independent form to include all of the limitations of the base claim, now canceled claim 46, claim 62 has been rewritten in independent form to include all of the limitations of the base claim, now canceled claim 46, and claim 74 has been rewritten in independent form to include all of the limitations of the base claim, now canceled claim 65, respectively, which make amended claims 30, 32, 57, 62 and 74 allowable.

Accordingly, amended claims 30, 32, 57, 62 and 74 are now allowable. Thus, claim 31, which is dependent from amended claim 30, claims 58-61, which are dependent from amended claim 57, claim 63, which is dependent from amended claim 62, and claim 75, which is dependent from amended claim 74, are also allowable.

Moreover, as amended, claims 47-56 and 64 are dependent from allowable claim 62, and thus are allowable at least for this reason.

Additionally, as amended, claims 66-73 and 76 are dependent from allowable claim 74, and thus are allowable at least for this reason.

In sum, as amended, per the Examiner's suggestions, claims 30-32, 47-64 and 66-76 are allowable.

B. 35 U.S.C. §102 Rejections

Claims 1, 2, 11, 15-17, 20-22 and 77-80 were rejected under 35 U.S.C. §102(b) as being anticipated by Hillenkamp. Furthermore, claims 1-5, 11, 12, 15-22, 46-48, 56, 64-67, 73 and 76-80 were rejected under 35 U.S.C. §102(e) as being anticipated by Hunter. Moreover, claims 1, 2, 11, 12, 15-17, 20-22 and 77-80 were rejected under 35 U.S.C. §102(b) as being anticipated by Krutchinsky. Applicants respectfully traverse the rejections made by the Examiner at least for the reasons discussed below.

Claims 1-16

Amended claim 1, among other unique limitations, recites a method for desorption and ionization of analytes comprising the steps of: "a. preparing a sample comprising *analytes* in a *medium* having at least one component; b. selecting a resonant *vibrational mode* of at least one

component of the medium; c. selecting a laser *tuned* to emit light substantially at the wavelength of the selected vibrational mode...” (Emphasis added.)

In one embodiment as shown in Fig. 1 of the present application as filed, for example, a sample 104 containing both ablation medium 108 and analyte components 110 is arranged on a support 102. A laser beam 106 from a laser (not shown) irradiates the sample 104 thereby causing to erupt from the sample a 107 plume containing ablated components of the medium 108 and both neutral 110 and ionized 112 analyte molecules. The analytes are laser desorbed directly from the medium without any application of exogenous matrix.

In contrast, Hillenkamp discloses a process for the laser desorption of analyte molecular ions, and suitable matrices for the process, where “[a]n additional point to be taken into account with these suitable matrices is that not only must the particular matrix be able to absorb in the selected wavelength range or at the selected wavelength in each case, ... but also that other properties ... contribute to the utilizability of a suitable absorbing matrix.” “These [properties] include, on the one hand, the *necessity* for matrix molecules to form a homogeneous mixture with the analyte molecules, even on evaporation of the solvent on introduction of the sample or the specimen into the vacuum, and not to segregate. On the other hand, the matrix molecules act as proton donors from the electronically excited state and thereby make the ionization of the analyte molecules possible in the first place.” Hillenkamp, col. 3, lines 29-46.

Therefore, Hillenkamp teaches away from the present invention as defined by amended claim 1 at least because (1) the sample must have analytes mixed with a matrix and a solvent, and (2) the process is conducted by selecting a laser emitting light with a selected wavelength range or selected wavelength and selecting a suitable matrix being able to absorb in the selected wavelength range or at the selected wavelength, not the one by selecting a resonant vibrational mode of at least one component of the medium and selecting a laser tuned to emit light

substantially at the wavelength of the selected vibrational mode according to amended claim 1 of the present invention.

In other words, in the Hillenkamp process, one must have a matrix and the matrix must be chosen to “match” the laser being use; while the present invention as defined by amended claim 1 requires no matrix and the laser was tuned to “match” a selected vibrational mode of the gel, which allows the present invention to be applied to a wide spectrum of medium.

Furthermore, Hunter discloses a method for matrix-assisted laser desorption/ionization mass spectrometry, where preparation of a sample of large organic molecules “typically includes providing a solution comprising a large organic molecule to be analyzed, a matrix molecule comprising a volatile, light-absorbing hydroxy-bearing matrix molecule, and a solvent, and evaporating the solvent to provide a solid crystalline matrix containing the molecule to be analyzed.” Hunter, col. 8, lines 9-16. Specifically, “[s]amples are prepared by dissolving the analyte in a solution containing the matrix molecule, with the bulk of the solution being one or more solvents which are subsequently allowed to evaporate before mass analysis begins.” Hunter, col. 9, lines 32-35. For desorption/ionization, laser “[w]avelength from the ultraviolet to infrared may be employed, depending on the cooled matrix being analyzed.” Hunter, col. 10, lines 34-35. And “[l]aser wavelengths of either 355 or 266 nm were employed for desorption/ionization in the examples...” Hunter, col. 11, lines 62-63.

Therefore, Hunter teaches away from the present invention as defined by amended claim 1 at least because (1) the samples in Hunter are prepared with an organic molecule, a matrix molecule and solvents, not the one only with analytes in a medium according to amended claim 1 of the present invention, and (2) the method of Hunter requires a step of selecting a laser emitting light with a fixed wavelength, not the one selecting a resonant vibrational mode of at least one component of the medium and selecting a laser tuned to emit light substantially at the

wavelength of the selected vibrational mode according to amended claim 1 of the present invention.

In other words, in the Hunter process, one must have a matrix and the matrix must be chosen to “match” the laser being use; while the present invention as defined by amended claim 1 requires no matrix and the laser was tuned to “match” a selected vibrational mode of the gel, which allows the present invention to be applied to a wide spectrum of medium.

Moreover, Krutchinsky discloses a time-of-flight mass spectrometry for a laser desorbed multiphoton ionization of GlnTrp and GlyTyr peptides and their mixture on two types of thin-layer chromatography (TLC) plates which are “silica gel ... and cellulose, ...[and] performed using two solvent systems...” Krutchinsky, page 375, right column, lines 28-34, and “a pulse CO₂ laser (Alltec 854) beam focused onto a 0.5 mm diameter spot desorbed a sample directly in front of an expanding gas jet.” Krutchinsky, page 376, right column, lines 26-28.

Therefore, Krutchinsky teaches away from the present invention as defined by amended claim 1 at least because (1) the sample in Krutchinsky is prepared with analytes (GlnTrp and GlyTyr peptides and their mixture) mixed with a matrix (silica gel and /or cellulose) and solvents, not the one only with analytes in a medium according to amended claim 1 of the present invention, and (2) the mass spectrometry of Krutchinsky is conducted by selecting a laser emitting light with a fixed wavelength which the matrix is able to absorb at, not the one by selecting a resonant vibrational mode of at least one component of the medium and selecting a laser tuned to emit light substantially at the wavelength of the selected vibrational mode according to amended claim 1 of the present invention.

Therefore, none of Hillenkamp, Hunter and Krutchinsky, taken alone or in combination, suggests or teaches a method for desorption and ionization of analytes comprising the steps of “a. preparing a sample comprising analytes in a medium having at least one component; b. selecting

a resonant vibrational mode of at least one component of the medium; c. selecting a laser tuned to emit light substantially at the wavelength of the selected vibrational mode...” according to amended claim 1 of the present invention.

For at least the foregoing reasons, independent claim 1, as amended, is patentable under 35 U.S.C. §102(b) and §102(e) over the cited reference.

Accordingly, claims 2-16, which depend from allowable claim 1, are patentable at least for the above reasons.

Claims 17-22

Claim 17, among other unique limitations, recites a system for desorption and ionization of analytes comprising “a. means for preparing a sample comprising analytes in a medium having at least one component; b. means for selecting a resonant vibrational mode of at least one component of the medium; c. means for tuning a laser to emit light substantially at the wavelength of the selected vibrational mode...” Thus, claim 17 recites a system using means-plus-function language corresponding to limitations recited in amended claim 1.

Thus, for incorporating herein the reasons set forth above with respect to why amended claim 1 is allowable, independent claim 17 is patentable under 35 U.S.C. §102(b) and §102(e) over the cited references as well.

Accordingly, claims 18-22, which depend from allowable claim 17, are patentable at least for the above reasons.

Amended Claims 77-80

Amended claim 77, among other unique limitations, recites a system for desorption and ionization of analytes comprising “a support for holding a sample ... wherein the support for

holding a sample of analytes includes means for moving the sample in a relative motion back and forth to the laser light to form a rastering trace such that the desorption and ionization of the analytes occur substantially at a same region in space.”

In one embodiment as shown in Fig. 2 of the present application as filed, for example, a support 202 is capable of movement, independent or jointly, in each of two directions x and y such that the separated analyte locations 210 may be each positioned for irradiation by the laser beam 206 which is not coplanar with the movement directions.

In contrast, as shown in Figs. 1-4, Hillenkamp discloses a device for the laser desorption of analyte molecule ions from a specimen having “a specimen support 10 which is arranged in the vacuum chamber of an ion source 11.” “The specimen support 10 acts as target for a laser beam 12 which is emitted by a laser 13.” Hillenkamp, col. 5, lines 42-46. Therefore, Hillenkamp teaches away from the present invention as defined by amended claim 77 at least because the support 10 of Hillenkamp is fixed, which cannot move the sample in a relative motion back and forth to the laser light according to amended claim 77 of the present invention.

Furthermore, Hunter discloses a device for matrix-assisted laser desorption/ionization mass spectrometry where “the sample is placed on a cooled sample *stage* in order to maintain a low vapor pressure of the sample in the vacuum chamber of the mass spectrometer.” Hunter, col. 8, lines 58-61. Therefore, Hunter teaches away from the present invention as defined by amended claim 77 at least because the sample *stage* in Hunter is ***fixed***, which cannot move the sample in a relative ***motion back and forth*** to the laser light according to amended claim 77 of the present invention.

Moreover, Krutchinsky discloses a device for a laser desorbed multiphoton ionization of GlnTrp and GlyTyr peptides and their mixture on two types of thin-layer chromatography (TLC) plates “by sequential scanning of the thin-layer chromatography plates versus the infrared laser

spot allowed imaging of the distribution profile of the compounds.” Krutchinsky, Abstract. Therefore, Krutchinsky teaches away from the present invention as defined by amended claim 77 at least because the thin-layer chromatography *plates* in Krutchinsky are *fixed*, which cannot move the sample in a relative *motion back and forth* to the laser light according to amended claim 77 of the present invention.

Therefore, none of Hillenkamp, Hunter and Krutchinsky, taken alone or in combination, suggests or teaches a system for desorption and ionization of analytes comprising “a support for holding a sample ... wherein the *support* for holding a sample of analytes includes means for moving the sample in a relative *motion back and forth* to the laser light to form a rastering trace such that the desorption and ionization of the analytes occur substantially at a same region in space” according to amended claim 77 of the present invention. (Emphasis added.)

For at least the foregoing reasons, independent claim 77, as amended, is patentable under 35 U.S.C. §102(b) and §102(e) over the cited reference.

Accordingly, claim 78 and amended claim 80, which depend from allowable claim 77, are patentable at least for the above reasons.

35 U.S.C. §103 Rejections

Claims 3-5, 18, 19, 46-48, 51-56, 64-67, 70-73 and 76 were rejected under 35 U.S.C. §103(a) as being unpatentable over Krutchinsky as applied to claims 1, 2, 11, 12, 15-17, 20-22 and 77-80 above, and further in view of Hunter as explained above. Furthermore, claims 6-10, 23-29 and 33-45 were rejected under 35 U.S.C. §103(a) as being unpatentable over Krutchinsky as applied to claims 1, 2, 11, 12, 15-17, 20-22 and 77-80 above, and further in view of Strahler. Moreover, claims 49-55 and 68-72 were rejected under 35 U.S.C. §103(a) as being unpatentable over Hunter as applied to claims 1-5, 11, 12, 15-22, 46-48, 56, 64-67, 73 and 76-80 above, and

further in view of Cramer. As set forth above, claims 2-10 are patentable at least because amended claim 1 is allowable, and claims 18 and 19 are patentable at least because claim 17 is allowable. For the rest of the claims, Applicants respectfully traverse the rejections made by the Examiner at least for the reasons discussed below.

Claims 23-29 and 33-39

Claim 23, among other unique limitations, recites a method for desorption and ionization of analytes comprising the steps of: “a. preparing a sample having *analytes* and a *polyacrylamide medium* having at least one component; b. selecting a resonant *vibrational mode* of at least one component of the medium; c. selecting a laser *tuned* to emit light substantially at the wavelength of the selected vibrational mode ...” (Emphasis added.)

In contrast, Krutchinsky discloses a time-of-flight mass spectrometry for a laser desorbed multiphoton ionization of GlnTrp and GlyTyr peptides and their mixture on two types of thin-layer chromatography (TLC) plates which are “silica gel ... and cellulose, ...[and] performed using two solvent systems...” Krutchinsky, page 375, right column, lines 28-34, and “a pulse CO₂ laser (Alltec 854) beam focused onto a 0.5 mm diameter spot desorbed a sample directly in front of an expanding gas jet.” Krutchinsky, page 376, right column, lines 26-28.

Therefore, Krutchinsky teaches away from the present invention as defined by claim 23 at least because (1) the sample of Krutchinsky is prepared with analytes (GlnTrp and GlyTyr peptides and their mixture) mixed with a matrix (silica gel and /or cellulose) and solvents, not the one only with analytes and a polyacrylamide medium according to claim 23 of the present invention, and (2) the mass spectrometry of Krutchinsky is conducted by selecting a laser emitting light with a fixed wavelength which the matrix is able to absorb at, not the one by selecting a resonant vibrational mode of at least one component of the medium and selecting a laser tuned to emit light substantially at the wavelength of the selected vibrational mode according to claim 23 of the present invention.

Furthermore, Strahler discloses a matrix-assisted laser desorption-ionization mass spectrometry for analyzing the charge-derivatization of peptides in polyacrylamide gels and membranes having “a perfusion approach in which solvent is passed through the gel/membrane to move analytes to one surface where matrix crystal formation will occur”, Strahler, page 117, left column, lines 25-28, and “a Voyager Elite reflection time-of-flight mass spectrometer ... equipped with a nitrogen laser (337 nm, 3 ns pulse).” Strahler, page 113, right column, lines 9-13.

Therefore, Strahler teaches away from the present invention as defined by claim 23 at least because (1) the sample of Strahler is prepared with analytes mixed with a matrix and solvents, not the one only with analytes and a polyacrylamide medium according to claim 23 of the present invention, and (2) the mass spectrometry of Strahler is conducted by selecting a laser emitting light with a fixed wavelength, not the one by selecting a resonant vibrational mode of at least one component of the medium and selecting a laser tuned to emit light substantially at the wavelength of the selected vibrational mode according to claim 23 of the present invention.

In other words, in Krutchinsky or Strahler, one must have a matrix and the matrix must be chosen to “match” the laser being use; while the present invention as defined by amended claim 1 requires no matrix and the laser was tuned to “match” a selected vibrational mode of the gel, which allows the present invention to be applied to a wide spectrum of medium.

Therefore, neither Krutchinsky nor Strahler, taken alone or in combination, suggests or teaches a method for desorption and ionization of analytes comprising the steps of “a. preparing a sample having *analytes* and a *polyacrylamide medium* having at least one component; b. selecting a resonant *vibrational mode* of at least one component of the medium; c. selecting a **laser tuned to** emit light substantially at the wavelength of the selected vibrational mode ...” according to claim 23 of the present invention. (Emphasis added.)

For at least the foregoing reasons, independent claim 23 is patentable under 35 U.S.C. §103(a) over the cited references.

Accordingly, claims 24-29 and 33-39, which depend from allowable claim 23, are patentable at least for the above reasons.

Claims 40-45

Claim 40, among other unique limitations, recites a system for desorption and ionization of analytes comprising “a. means for preparing a sample having analytes and a polyacrylamide medium having at least one component; b. means for selecting a resonant vibrational mode of at least one component of the medium; c. means for tuning a laser to emit light substantially at the wavelength of the selected vibrational mode ...” Thus, claim 40 recites a system using means-plus-function language corresponding to limitations recited in amendment claim 23.

Thus, incorporating herein the reasons set forth above with respect to why amendment claim 23 is allowable, independent claim 40 is patentable under 35 U.S.C. §103(a) over the cited references as well.

Accordingly, claims 41-45, which depend from allowable claim 40, are patentable at least for the above reasons.

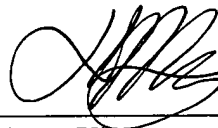
CONCLUSION

Applicants respectfully submit that the foregoing Amendment and Response place this application in condition for allowance. If the Examiner believes that there are any issues that can be resolved by a telephone conference, or that there are any informalities that can be corrected by an Examiner's amendment, please call the undersigned at 404.954.5088.

Appl. No. 09/931,490
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No fees are believed due; however the commissioner is authorized to charge any fee due or refund any credit to Deposit Account No. 13-2725.

Respectfully submitted,
MERCHANT & GOULD



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